

## REMARKS

### A. Status of the Claims

Claims 1-3 are rejected in the present Office Action. No claims are amended, added, or canceled herein. Applicants thank the Examiner for the previous consideration of our submissions.

### B. Rejection under 35 U.S.C. §103

The Action rejects all claims under 35 U.S.C. 103(a) as being obvious over Malfroy-Camine *et al.* (6,064,188) in view of Winkler *et al.* (Molecular Vision 1999). Malfroy-Camine *et al.* is said to teach the antioxidant and superoxide dismutase activity of the claimed compounds. Winkler *et al.* is said to teach the role of oxidation in relation to macular degeneration and suggest that superoxide dismutase activity may be involved in preventing oxidative damage. The Action suggests that the combination of these references would have made obvious to one skilled in the art the use of the claimed compounds having superoxide dismutase activity for the treatment of conditions associated with oxidative damage such as AMD. Applicants respectfully traverse.

Applicants thank the Examiner for considering the De La Paz and Delcourt references discussed in the Response to the Office Action Mailed June 14, 2007. In the present Action, the Examiner indicates that Applicants' arguments relative to the two references are not well taken. In particular, the Action appears to assert that Applicants' main argument with respect to the two references relied on the lack of teaching that superoxide can be used to treat macular degeneration. Further, the Action states that "the fact that the references recognize that superoxide dismutase is involved in protecting against oxidative damage such as that which leads to AMD, is sufficient for a person skilled in the art to use such compounds for the treatment of AMD." Applicants respectfully submit that De La Paz *et al.* and Delcourt *et al.* do not actually support the Action's assertions, and Applicants apologize if their previous arguments lead the Examiner to such a conclusion. Applicants hope that the discussion below will clarify the teachings of De La Paz *et al.* and Delcourt *et al.*, and demonstrate that the claims are not obvious over Malfroy-Camine *et al.* in view of Winkler *et al.*

The Action asserts that one of skill in the art would have been motivated to combine the teachings of Malfroy-Camine *et al.* in view of Winkler *et al.*, because one of them teaches that the claimed compounds have superoxide dismutase activity, and the other allegedly relates to the use of superoxide dismutase compounds for the treatment of macular degeneration.

The Action asserts that Winkler *et al.* suggests that there is a correlation between oxidation and macular degeneration and the use of superoxide dismutase in preventing oxidative damage caused by macular degeneration. Applicants recognize that obviousness does not require absolute predictability, as pointed out on page 5 of the Action. However, as stated in MPEP §2143.02 (II):

The test for obviousness is what the combined teachings of the references would have suggested to one of ordinary skill in the art, and all teachings in the prior art must be considered to the extent that they are in analogous arts. Where the teaching of two or more prior art references conflict, the examiner must weigh the power of each reference to suggest solutions to one of ordinary skill in the art, considering the degree to which one reference might accurately discredit another.

Although Winkler *et al.* suggest, without any data to support the suggestion, that superoxide dismutase may be useful in protecting against macular degeneration, there were teachings in the art at the time the instant application was filed that conflicted with the teaching in Winkler *et al.* In particular, De La Paz *et al.* (1996, *Br. J. of Ophthalmology* 80:445-450) and Delcourt *et al.* (1999, *Ophthalmology* 106:215-221) both involve research studies in which blood samples were taken from a group of participants in order to statistically analyze the levels of superoxide dismutase activity in comparison to the severity of AMD. The De La Paz study included 66 participants, 54 of whom showed varying levels of severity of aging maculopathy. The paper concluded based on multiple regression analysis and ordinal logistic regression analysis ***that there is no significant association between disease severity of AMD and superoxide dismutase activity.*** The Delcourt study included 2,156 participants for its analysis of AMD and antioxidant enzymes, 38 of whom had late AMD. The paper concluded, based on similar statistical analyses, that high levels of erythrocyte superoxide dismutase activity ***were not associated with late AMD and early signs of AMD.***

The instant claims relate to *treating* persons suffering from the exudative and non-exudative forms of AMD, diabetic retinopathy, which includes proliferative diabetic retinopathy, or retinal edema. Both De La Paz and Delcourt provided statistical data that higher levels of the enzyme do not correspond to the severity of AMD, which suggests that an increase in the amount of the superoxide dismutase would have no effect in treating AMD, because there is no association between the severity of AMD and the amount of superoxide dismutase activity. Thus, these papers appear to teach away from the use of superoxide dismutase for *treating* macular degeneration.

Winkler *et al.* do not provide or discuss any data to refute the data or conclusions of De La Paz *et al.* or Delcourt *et al.*

Consequently, one of skill in the art would not have been motivated to use compounds with superoxide dismutase activity for treating macular degeneration, since there would have been no reasonable expectation that the use of such compounds for that purpose would be successful based on the studies discussed in De La Paz *et al.* and Delcourt *et al.*

In conclusion, the combination of teachings of the cited references does not teach or suggest the use of the claimed compounds for treating macular degeneration, diabetic retinopathy, or retinal edema, and there would have been no reasonable expectation of success with respect to such use in view of the totality of the art at the time the instant application was filed.

In light of the foregoing arguments, Applicants respectfully request that the obviousness rejection be withdrawn.

### **C. Double Patenting**

Claims 1-3 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being allegedly unpatentable over claims 1-7 of co-pending Application No. 10/729,222. Applicants are filing herewith a terminal disclaimer, thereby overcoming the double patenting rejection.

**D. Conclusion**

This is submitted to be a complete response to the outstanding Action. The Examiner is invited to contact the undersigned attorney at (817) 615-5330 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

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Date: June 25, 2008